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EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Application No.	Applicant(s)	
10/619,539	BOSCH ET AL.	
Examiner	**Art Unit**	
Susan T. Tran	1615	

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-123* is/are pending in the application.

4a) Of the above claim(s) *46-123* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/09/07;08/27/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-40, 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The claims are rejected because they do not identify the structure, material, or acts set forth in the specification that would be capable of carrying out the functional properties recited in the claims. It appears that the specification does not provide adequate teaching and/or support as to how the composition can result in the claimed release profile, C_{max}, Tmax, and bioequivalency. Accordingly, the structure which makes up the formulation must be clearly and positively specified.

Claims 35-40, 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims lack the description of the possible genus with the recited functional characteristics.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 13, 24, 32-35, 37 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 contains the trademark/trade name "POLYQUAT ™" or "MIRAPOL™" or "ALKAQUAT™". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name.

Claim 13 recites the limitation "the liquid media of the liquid dosage composition" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claims 32-34 recite the limitation "the viscosity" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 35 recites the limitation "the T_{max}" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 37 recites the limitation "the C_{max}" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 39 recites the limitation "the AUC" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 10-15, 18 and 20-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Na et al. US 5,298,262.

Na discloses a composition comprising active-containing nanoparticles having a surface modifier adsorbed on the surface thereof and a non-ionic cloud point modifier associated therewith (abstract). Column 2, line 1 through column 3, lines 1-11, disclosed the claimed surface modifier. Surface modifier is used in an amount 0.1-90% (column 4, lines 53-68). The composition further comprises isotonicity maintaining compounds include mannitol, dextrose, and sodium chloride (crystal growth inhibitor) (column 6, lines 29-32). Na further teaches the nanoparticle has an effective average particle size of less than about 400 nm (column 5, lines 8-28).

Claims 1-5, 8-15 and 17-24 are rejected under 35 U.S.C. 102(b) as being anticipated by Na et al. EP 0601619 (Na 2).

Na discloses a nanoparticulate composition comprising active agent, surface modifier adsorbed on the surface thereof and 0.01-50% of a non-ionic cloud point modifier (crystal growth inhibitor) (abstract; and page 5, lines 26-27). Surface modifier is disclosed in page 2, lines 54 through page 3, lines 1-34. Na further discloses the use of two or more surface modifier (page 3, lines 34-35). Cloud point modifier includes glycerol (page 5, lines 15-18).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Na and Na 2, in view of Liversidge US 2005/0004049.

Na and Na 2 are relied upon for the reasons stated above. The cited references do not explicitly teach the claimed active agent, as well as the claimed properties, such as Cmax, Tmax, bioequivalent, and viscosity.

Liversidge teaches a nanoparticulate composition comprising surface modifier, and a drug having solubility of less than about 30 mg/ml (abstract; and paragraph 0045). Drug including analgesic, NSAID and vitamins are discloses in paragraphs 0109-0113). The claimed surface modifier, and combination of two or more surface modifier is disclosed in paragraphs 0124-0144). Liversidge also teaches the claimed

effective particle size in paragraphs 0161-0162. The nanoparticulate composition is processed into a liquid dosage for bioadhesive composition (paragraphs 0081-0089). Liversidge further teaches the claimed viscosity, Cmax, Tmax, and bioequivalency (paragraphs 0090-0105). Thus, it would have been obvious to one of ordinary skill in the art to modify the nanoparticulate compositions of Na and Na 2 in view of the teachings of Liversidge to obtain the composition, because Liversidge teaches a nanoparticulate composition that is advantageous to a pharmaceutical art, such as improve clinical efficacy, reduce fed/fasted variability, and potentially reduce side effects (paragraph 0028), because Na and Na 2 teach a nanoparticulate composition suitable for a variety of drugs, and because Na and Na 2 teach the desirability to obtain a nanoparticulate composition useful in pharmaceutical art.

Response to Arguments

Applicant's arguments filed 07/09/07 have been fully considered but they are not persuasive.

The 112, first paragraph rejection:

Applicant argues that the specification teaches that "by decreasing the particle size of an active agent, the surface area of the composition is increased, thereby generally resulting in an increased bioavailability" and that "[the] nanoparticulate active agents must be physically stable." See, for example, at page 1, lines 16-21; at page 4, lines 23-28; at page 5, lines 15-24; and at page 12, lines 3-10. By definition, "bioavailability" is a measurement of the rate and extent of a therapeutically active drug that reaches the

systemic circulation and is available at the site of action (online Wikipedia encyclopedia). The skilled artisan would have appreciated that bioavailability is determined by a pharmacokinetic study and represented by the plasma drug concentration *vs.* time after administration. The specification further describes that bioequivalency "is preferably established by a 90% Confidence Interval (CI) of between 0.80 and 1.25 for both C_{max} and AUC" (page 18, lines 18-25). Therefore, the specification provides written support that to achieve the claimed release profile, represented by the C_{max}, T_{max}, AUC and bioequivalency, the active ingredient must be reduced to an average particle size of less than 2000 nm and be maintained stable at this size in the presence of at least one surface stabilizer and at least one osmotically active crystal growth inhibitor, as recited in claim 1. The specification is also enabling because it describes how to make nanoparticulate formulations (page 32ff) and how the composition is stabilized in the presence of different crystal growth inhibitors (Examples 1-8).

In response to applicant's argument, it is noted that although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, it appears from the present specification that the specific C_{max} and T_{max} are obtained from formulations with specific ratios between the active agent: surface-active agent: active crystal growth inhibitor. However, those limitations are not even recited in the rejected claims. If one of ordinary skill in the art was by routine experimentation to make and use the claimed invention, the skilled artisan would have to go through

burdensome amount of experimentation to combine different ratios of the three components. Accordingly, the 112, first paragraph rejection is maintained.

Applicant argues that both of the Na references are intended to solve the problem of "aggregation of nanoparticles upon heating" (column 1, lines 26-31) by introducing into the composition a cloud point modifier, which functions to "increase the cloud point of the surface modifier" (column 1, line 66 to column 2, line 3; column 6, lines 2-11). By contrast, the claimed invention is irrelevant to elevating the cloud point of the surface stabilizer. Rather, the claimed invention is directed to the discovery that an osmotically active crystal growth inhibitor can prevent crystal growth of the nanoparticulate active agent particles *at ambient temperatures. See,* for examples, at page 21, line 20. The working examples of the present application all speak to increased stability of a composition comprising an osmotically active crystal growth inhibitor at room temperature or at 40°C.

However, in response to applicant's argument, although the Na references teach the use of a "cloud point modifier", the "cloud point modifier" taught by Na is sorbitol, which is the same the sorbitol claimed by applicant as an active crystal growth inhibitor. Accordingly, the burden is shifted to applicant to show that the sorbitol taught by the Na references is different sorbitol being claimed. An applicant is entitled to be his or her own lexicographer and may rebut the presumption that claim terms are to be given their ordinary and customary meaning by clearly setting forth a definition of the term that is different from its ordinary and customary meaning(s). See *In re Paulsen*, 30 F.3d 1475, 1480, 31 USPQ2d 1671, 1674 (Fed. Cir. 1994) (inventor may define specific terms used

to describe invention, but must do so "with reasonable clarity, deliberateness, and precision" and, if done, must "set out his uncommon definition in some manner within the patent disclosure' so as to give one of ordinary skill in the art notice of the change" in meaning) (quoting Intellicall, Inc. v. Phonometrics, Inc., 952 F.2d 1384, 1387-88, 21 USPQ2d 1383, 1386 (Fed. Cir. 1992)).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan T. Tran whose telephone number is (571) 272-0606. The examiner can normally be reached on M-F 6:00 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SUSAN TRAN
PRIMARY EXAMINER

Art Unit 1615